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October 3, 2002

PATENT APPLICATION
Attorney's Docket No.: 1159.1006-007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Steven A. Bogen, Herbert H. Loeffler and John A. Purbrick

Application No.: 09/688,619

Group: 1743

Filed: October 16, 2000

Examiner: J. Snay

For: Random Access Slide Stainer with Independent Slide Heating Regulation

A. Lawrence
Suppl. Patent
10-4-02

VIA HAND DELIVERY

SUPPLEMENTAL AMENDMENT

Assistant Commissioner for Patents
P.O. Box 2327
Arlington, VA 22202

Sir:

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Applicant thanks Examiner Snay for a very helpful interview with Dr. Bogen and the undersigned. The following amendments and remarks address issues which arose during that interview, and it is believed that the amendments will place the application in condition for allowance.

Please amend the application as follows:

In the Claims

Please cancel Claim 3.

Please amend Claims 1, 2, 5, 6 and 8. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - ii).

CLAR

(Thrice Amended) A method of processing samples mounted on microscope slides as claimed in claim 1 further comprising:

23

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09/688,619

-2-

communicating data from a computer not located on the moving platform to electronic circuitry mounted on the moving platform; and

processing the data in the electronic circuitry on the moving platform and supplying, from the electronic circuitry on the moving platform, amounts of electrical power to the heating elements dependent on the data, to heat one of the slides to a different temperature than a second one of the slides.

C1

C2/52

(Twice Amended) A method of processing samples mounted on microscope slides as claimed in claim ⁴1, wherein each heating element heats only one slide.

C3

(Twice Amended) A method of processing samples mounted on microscope slides as claimed in claim ³1 further comprising;

providing a computer comprising a user interface through which a desired temperature for each microscope slide is specified, said user interface being mounted off of the moving platform;

C3

sending data from the computer to the electronic circuitry on the moving platform over a group of conductors, the number of conductors in said group of conductors being less than the number of heating elements controllable to individual temperatures; and

processing the data in the electronic circuitry on the moving platform, and supplying electrical power to the heating elements from the electronic circuitry on the moving platform.

C4

C2/1

(Amended) A method of processing samples mounted on microscope slides comprising:

placing two or more microscope slides on a platform;

providing heating elements capable of heating said slides, said heating elements being under independent electronic control and thereby capable of heating some slides to a different temperature than other slides;

moving the platform and a liquid dispenser relative to each other;

dispensing liquid from the dispenser onto the slides; and

on the platform, heating one slide to a different temperature than a second slide.

09/688,619

-3-

3.2. (Amended) A method of processing samples mounted on microscope slides as claimed in claim 1, wherein the platform is a moving platform capable of indexing slides adjacent to a stationary liquid dispensing location.

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REMARKS

Claims 1, 2 and 5 stand rejected under 35 U.S.C. 103 as being unpatentable over Bogen, *et al.* ('114) in view of Muller, *et al.* ('905) or Potter, *et al.* ('842) and further in view of Horne ('299). Claims 6-9 were presented in the last amendment and were discussed in the interview.

As was discussed in the interview, a class of biological analysis which has been successfully implemented using carousel type slide carriers is that of immunohistochemistry (IHC). Carousel systems provide particular advantage when used with IHC techniques because they permit slides to be indexed to dispensing stations where small volumes of reagent may be dispensed onto the slides.

Ventana Medical Systems Inc. has been a principal provider of such carousel systems. A Ventana patent to Richards, *et al.* (6,296,809), though not prior art to the present application, provides an extensive discussion in its background, including a discussion of IHC techniques. As noted in Richards, *et al.*, such systems typically allow for heating of all slides to 37 degrees C, matching body temperature (see column 1, lines 64 and 65 and column 2, lines 22-28). Hot air blower and heat lamp heating of the samples used in prior Ventana systems is noted at column 2, lines 22-23, and the resistive heating elements of Bogen, *et al.* (5,645,114) are discussed at lines 50-59.

The present invention was developed to address the needs of another class of biological analysis, generally referred to as special stain techniques, for which carousel systems had not previously been used. Prior to automation, special stain techniques often required judgments on the part of the technician, such as color analysis. Namely, the technician dipped the slide in a chemical or dye until the tissue elements acquired a certain specified color, as determined visually. Examples of special stain processes are presented in Exhibits A, B and C. In those

25

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09/688,619

-4-

exhibits, arrows with asterisks indicate steps in the procedures which must be performed visually and thus require user input. Because such techniques rely highly on the skills of the technician, and are considered an art, they had not been considered appropriate for automatic processing using a carousel type system.

Applicants recognized that even special stain processes could be performed in an automated system by strictly controlling variables such as reagent concentration (requiring use of reagent only once), temperature and incubation time. Contrary to beliefs of those skilled in the art, precise control could take the place of the art required prior to the present invention.

Proper automation of special stains required not only the ability to obviate the need for human visual interpretation, but also the ability for a single instrument to heat different slides to different temperatures for varying periods of time. For example, in Exhibits A-C, note the different temperatures indicated by arrows and circles. Thus, to provide an automated system for special stain processing, applicants additionally provided independent electronic control of heating elements in order to heat slides to different temperatures. That feature had not previously been included in systems that enabled controlled dispensing of minute volumes of reagent on slides by indexing the slides relative to reagent dispensers.

In fact, two years after the priority date of the present application, Ventana Medical Systems published the attached article, Exhibit D, (Grogan, Thomas, et al. "An Update on "Special Stain" Histochemistry with Emphasis on Automation," *Advances in Anatomic Pathology*, Vol. 7, No. 2, pp. 110-122), which discusses the "art" of special stain techniques (page 120) as well as the difficulties of automating special stain processing (pages 117-118). The Ventana proposal was to adapt all special stains to a single processing temperature (page 117). They relied on a dry forced air heater capable of heating all samples to 60°C (pages 118-119).

Amended independent claim 6 recites independent temperature control of slides in a system in which a liquid dispenser and a slide supporting platform are moved relative to each

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09/688,619

-5-

other in order to dispense liquid on the slide. None of the prior art, alone or in combination, teaches such a system.

Muller, *et al.* is a very different type of system which, as previously discussed, is not compatible with systems having indexing between the slides and a dispenser to dispense liquid onto the slides. Muller, *et al.* relates to a class of analysis that uses expensive reagents and heats to high temperatures. As a result, samples are enclosed in small chambers in order to prevent evaporation of the reagent. Muller, *et al.* used a syringe to manually inject small quantities of reagent into the chambers. By contrast, in Bogen, *et al.* the slides are exposed (not sealed in a chamber) so that reagent can be dropped from a dispenser onto a desired slide that was indexed to the dispenser. Thus, Muller, *et al.* would not, and could not, be combined with Bogen, *et al.* to provide the system recited in claim 6.

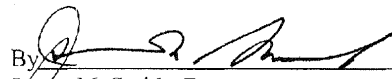
With respect to claims 1, 2 and 5, which have been placed in dependent form, please refer to the arguments presented with the last amendment.

Examiner Snay indicated that the Patent Office file did not include the Answer to the Complaint which was noted in the last Amendment. A copy of that document is attached.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, he is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,
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Concord, MA 01742-9133

Dated: 10/5/2

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09/688,619

-i-

MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

1. (Thrice Amended) A method of processing samples mounted on microscope slides as claimed in claim 8 further comprising:
 - [placing two or more microscope slides on a moving platform, the moving platform having heating elements thereon to heat said slides;]
 - communicating data from a computer not located on the moving platform to electronic circuitry mounted on the moving platform; and
 - processing the data in the electronic circuitry on the moving platform and supplying, from the electronic circuitry on the moving platform, amounts of electrical power to the heating elements dependent on the data, to heat one of the slides to a different temperature than a second one of the slides.
2. (Twice Amended) A method of processing samples mounted on microscope slides as claimed in claim 1, wherein each heating element[s] heats only one slide.
5. (Twice Amended) A method of processing samples mounted on microscope slides as claimed in claim 8 further comprising:
 - [positioning a plurality of microscope slides bearing biologic samples on a moving platform, said moving platform having a plurality of heating elements controllable to individual temperatures and electronic circuitry thereon;]
 - providing a computer comprising a user interface through which a desired temperature for each microscope slide is specified, said user interface being mounted off of the moving platform;
 - sending data from the computer to the electronic circuitry on the moving platform over a group of conductors, the number of conductors in said group of conductors being less than the number of heating elements controllable to individual temperatures; and
 - processing the data in the electronic circuitry on the moving platform, and supplying electrical power to the heating elements from the electronic circuitry on the moving platform.

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09/688,619

-ii-

6. (Amended) A method of processing samples mounted on microscope slides comprising:
 - placing two or more microscope slides on a [moving] platform;
 - providing heating elements capable of heating said slides, said heating elements being under independent electronic control and thereby capable of heating some slides to a different temperature than other slides; [and]
 - moving the platform and a liquid dispenser relative to each other;
 - dispensing liquid from the dispenser onto the slides; and
 - on the [moving] platform, heating one slide to a different temperature than a second slide.

8. (Amended) A method of processing samples mounted on microscope slides as claimed in claim 6, wherein the platform is a moving platform [is] capable of indexing slides adjacent to a stationary liquid dispensing location.

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